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|---|---|-------------------------------------|---|--|--|--|--|--|
| _Date of  | Deposit: July 12, 2006  |                                     | Label Number:   | EV 768765377US                             |  |  |  |  |
| I hereby certify under 37 C.F.R. § 1.10 that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee" with sufficient postage on the date indicated above and is addressed to Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450. |   |                                     |   |  |  |  |  |  |
| Elvis   | De La Cruz  |                                     |   | 1  |  |  |  |  |
| Printed   | Printed name of person mailing correspondence Signature of person mailing correspondence  |                                     |   |  |  |  |  |  |
| Substit   | Substitute Form PTO 1390 U.S. Department of Commerce Patent and Trademark Office Attorney Docket Number:  |                                     |   |  |  |  |  |  |
| TRANSMITTAL LETTER TO THE UNITED STATES  DESIGNATED/ELECTED OFFICE (DO/EO/US)  CONCERNING A FILING UNDER 35 U.S.C. § 371  |   |                                     |   |  |  |  |  |  |
| INTERNATIONAL APPLICATION NUMBER  |   |                                     | INTERNATIONAL FILING DATE   | PRIORITY DATE CLAIMED                      |  |  |  |  |
| PCT/C   | A05/00040   |                                     | January 12, 2005  | January 12, 2004                           |  |  |  |  |
| REDI  |   |                                     | TISENSE OLIGONUCLEOTIDES DIRECTED TO RIBONUCLEOTIDE<br>DUCATASE R2 AND USES THEREOF IN COMBINATION THERAPIES FOR<br>E TREATMENT OF CANCER |  |  |  |  |  |
| APPLI   | CANTS FOR DO/EO/US:   | Aiping H                            | H. YOUNG, Jim A. WRIGHT, and Yoon LEE   |  |  |  |  |  |
| Applic  | ant herewith submits to the U   | nited State                         | s Designated/Elected Office (DO/EO/US)  | the following items and other information: |  |  |  |  |
| 1.  | ■ This is a FIRST submission of items concerning a filing under 35 U.S.C. § 371.  |                                     |   |  |  |  |  |  |
| 2.  | □ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. § 371.   |                                     |   |  |  |  |  |  |
| 3.  | ■ This is an express request to begin national examination procedures (35 U.S.C. § 371(f)).   |                                     |   |  |  |  |  |  |
| 4.  | ■ The U.S. has been elected.  |                                     |   |  |  |  |  |  |
| 5.  | A copy of the International Application (35 U.S.C. § 371(c)(2)).  a. is transmitted herewith (required only if not transmitted by the International Bureau).  b. has been transmitted by the International Bureau.  c. Is not required, as the application was filed with the United States Receiving Office (RO/US). |                                     |   |  |  |  |  |  |
| 6.  | An English language translation of the International Application into English (35 U.S.C. § 371(c)(2)).  |                                     |   |  |  |  |  |  |
|   | □ a. is transmitted herewith. □ b. has been previously submitted under 35 U.S.C. 154(d)(4).   |                                     |   |  |  |  |  |  |
| 7.  | Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. § 371(c)(3)).   |                                     |   |  |  |  |  |  |
|   | □ a. are transmitted herewith (required only if not transmitted by the International Bureau). □ b. have been transmitted by the International Bureau.   |                                     |   |  |  |  |  |  |
|   | <ul> <li>b. have been transmitted by the international Bureau.</li> <li>c. have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d. have not been made and will not be made.</li> </ul>  |                                     |   |  |  |  |  |  |
| 8.  | ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. § 371(c)(3)).   |                                     |   |  |  |  |  |  |
| 9.  | ■ An oath or declaration of the inventors (35 U.S.C. § 371(c)(4)). (unsigned)   |                                     |   |  |  |  |  |  |
| 10.   | □ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. §371 (c)(5).   |                                     |   |  |  |  |  |  |
| 11.   | ■ An Information Disclosure Statement under 37 C.F.R. §§ 1.97 and 1.98.   |                                     |   |  |  |  |  |  |
| 12.   | □ An assignment for recording. A separate cover sheet in compliance with 37 C.F.R. §§ 3.28 and 3.31 is included.  |                                     |   |  |  |  |  |  |
| 13.   | ■ A preliminary amendment.  |                                     |   |  |  |  |  |  |
| 14.   | □ A substitute specification  | ١.                                  |   |  |  |  |  |  |
| 15.   | □ A power of attorney and   | or change                           | of address letter.  |  |  |  |  |  |
| 16.   | □ Request for Deferred Ex   | □ Request for Deferred Examination. |   |  |  |  |  |  |
| 17.   | ■ Application Data Sheet.   |                                     |   |  |  |  |  |  |
| 18.   | ■Other items or information: Statement Under 37 C.F.R. § 1.821 (2 pgs.); Sequence Listing ( 26 pgs.); Sequence Diskette; IB308 (1 page); PCT/RO/101 (4 pages).  |                                     |   |  |  |  |  |  |

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## JAP20 Rec'd PCT/PTO 12 JUL 2006

| 19.    ■ The follo                       | wing fees are submitte   | ed:  |            |                       |     |
|--|--|--|------------|-----------------------|-----|
| Basic National Sta                       | ge Fee: \$300  | \$300.00   |            |                       |     |
| National Stage Se                        | arch Fee   | \$400.00   |            |                       |     |
|  | F.R. § 1.445(a)(2)) has<br>JSPTO as an Internati                               |  |            |                       |     |
| International Searc                      | h Report prepared an   |  |            |                       |     |
| All other situations                     | : \$500  |  |            |                       |     |
| National Stage Ex                        | amination Fee  | \$200.00   |            |                       |     |
|  | iminary examination ros<br>of PCT Articles 33(1)                               |  |            |                       |     |
| All other situations                     | : \$200  |  |            |                       |     |
|  | for furnishing the oath d priority date (37 C.F.                               | \$   |            |                       |     |
| CLAIMS                                   | NUMBER FILED   | NUMBER EXTRA   | RATE       |                       |     |
| Total claims                             | 38 - 20 =  | 18   | x \$50     | \$900                 |     |
| Independent claim                        | s 4-3=   | 1  | x \$200    | \$200                 |     |
| Multiple dependen                        | t claims (if applicable)   |  | + \$360    | \$                    | - " |
| 100 sheets (exclud                       | ee: Additional fee for s<br>ling sequence listing o<br>). The fee is \$250 for |  |            |                       |     |
| TOTAL SHEETS                             | EXTRA SHEETS   | Number of each additional 50 sheets or fraction thereof (round up to a whole number) | RATE       |                       |     |
| -100=                                    | /50=   |  | X\$250     | \$250.00              |     |
|  |  | LCULATIONS =   | \$2,250.00 |                       |     |
| Reduction of 1/2 for entity status under | or filing by small entity,<br>37 C.F.R. § 1.27                                 | \$   |            |                       |     |
|  |  | \$   |            |                       |     |
| Processing fee of months from the e      | \$130.00 for furnishing arliest claimed priority                               | \$   |            |                       |     |
|  |  | \$ 2,250.00  |            |                       |     |
|  | he enclosed assignmented by an appropriate y.                                  | \$   |            |                       |     |
|  |  | \$ 2,250.00  |            |                       |     |
|  |  |  |            | Amount to be refunded | \$  |
|  |  |  |            | charged               | \$  |

- a. A check in the amount of \$2,250.00 to cover the above fees is enclosed.
- $\square$  b. Please charge my Deposit Account No. 03-2095 in the amount of \$ [\*\*] to cover the above fees.
- ☑ c. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 03-2095.

NOTE: Where an appropriate time limit under 37 C.F.R. §§ 1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. § 1.137(a) or (b) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Kristina Bieker-Brady, Ph.D. Clark & Elbing LLP 101 Federal Street Boston, MA 02110-2214

Telephone: 617-428-0200 Facsimile: 617-428-7045 Customer No.: 21559

Signature Kristiya Bieker-Brady, Ph.B.

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|                                | nce is being deposited with the United States Postal Service as ostage on the date indicated above and is addressed to Commissioner Signature of person melling correspondence |  |  |  |  |  |
|                                |  |  |  |  |  |  |

## **APPLICATION**

## FOR

## UNITED STATES LETTERS PATENT

APPLICANTS: Aiping H. YOUNG, Jim A. WRIGHT, and Yoon LEE

TITLE: ANTISENSE OLIGONUCLEOTIDES DIRECTED TO

RIBONUCLEOTIDE REDUCATASE R2 AND USES THEREOF IN COMBINATION THERAPIES FOR THE

TREATMENT OF CANCER